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Kagan Binder, PLLC 221 Main Street North Suite 200 Stillwater, MN 55082			EXAMINER CARTER, KENDRA D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of February 1, 2008 made to the office action filed July 26, 2007. Claims 1-6, 8, 11, 20, 27, 30 and 58-64 are pending. Claims 1 and 8 are amended and claims 58-64 are new. Claims 7, 9, 10, 12-19, 21-26, 28, 29 and 31-57 are cancelled.

In light of the amendments, the following rejections are withdrawn: 1) the 35 USC 112, second paragraph rejection of claims 19 and 29; 2) the 35 U.S.C. 102(b) rejection of claims 1-4, 6, 7, 9-12, 14-18, 20, 25-30, 45 and 46 as being anticipated by Wong et al.; 3) the 35 U.S.C. 102(b) rejection of claims 1, 3-5, 7, 9-12, 14-20, 25-29 and 45 as being anticipated by Hughes et al.; and 4) the 35 U.S.C. 103(a) rejection of claims 5 and 19 as being unpatentable over Wong et al. as applied to claims 1-4, 6, 7, 9-12, 14-18, 20, 25-30, 45 and 46 above in view of Hughes et al. as applied to claims 1, 3-5, 7, 9-12, 14-20, 25-29 and 45 above.

The Applicant's arguments of the 35 USC 112, second paragraph rejection of claim 5 was found persuasive, and thus withdrawn.

For the reasons in the previous office action and below, the Applicant's arguments of the 35 USC 103(a) rejection of claims 1, 7, 8 and 11-13 as being

unpatentable over Louis in view of Wong et al. in further view of Hughes et al. were found not persuasive.

In regards to the apparent typo of typing in the wrong patent number for Hughes has been corrected in the action below. The Examiner cited the correct patent number on the PTO-892 form as US-5,962,027.

Due to the amendment to the claims, the new and modified 35 U.S.C. 102(b) and 103(a) rejection are made below. The Applicant's arguments pertaining to the maintained rejection is addressed below, the arguments directed towards the withdrawn claims due to amendment of the claims are moot in light of the new rejections.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Wong et al. (US 5,632,984; referred to as Wong'984).

Wong'984 teaches intraocular administration of drugs that concentrate the drug at the site of the disease and where biodegradable microcapsules are employed, providing continuous, long-lasting treatment (see abstract and column 3, lines 8-9). The administration is into the posterior segment of the eye allowing diffusion of the drug throughout the vitreous within the posterior segment, and further into the entire retina, the choroid and the opposed sclera (i.e. instilling therapeutic medium sub-retinally; see column 4, lines 1-9; addresses claim 1). Administration may be achieved by injection in a saline solution (see column 7, lines 63-65 and column 9, lines 63-67).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(1) Claims 1-4, 6, 7, 8, 11, 20, 27, 58-61, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. (US 5,869,079) in view of Wong et al. (US 5,632,984; referred to as Wong'984).

Wong et al. teaches combinations of hydrophilic and hydrophobic entities in a biodegradable implants that provide controlled, sustained drug release for an extended period of time (see abstract in its entirety; addresses claims 27 and 64). Therapeutically active hydrophobic agents, which benefit from release include, non-steroidal anti-inflammatory drugs and steroids of particular interest including cortisone, prednisolone, dexamethasone, fluorometholone (see column 2, lines 63 and 64 to column 3, lines 1-5 and column 8, example 1, lines 23-25; addresses claims 3, 4, 60 and 61). The formulation of implants if for use in the treatment of ocular conditions, diseases, tumors and disorders are of particular interest (see column 6, lines 27-29). Implants are introduced into the suprachoroid may deliver drugs to the choroids and the anatomically apposed retina (i.e. localizing the action of the therapeutic medium at the choroids and the retina and minimizing action at other tissues of the eye and forming a depot of a drug between the choroids and the retina; see column 6, lines 38-40; addresses claims 2, 6, 8, 30 and 58). Suitable sites include the posterior chamber with a sub-retinal implantation (see column 6, lines 32, 33 and 61, and 62; addresses claims 1, 11, 20, 27, 58, 63 and 64). The implants may be administered by surgical means, injection or trocar (see column 7, lines 15 and 16; addresses claims 1 and 20). The implants may

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have the active agent homogenously distributed through the polymeric matrix, or encapsulated, where a reservoir of active agent is encapsulated by the polymeric matrix (i.e. core comprising a biocompatible matrix and therapeutic medium; see column 5, lines 19-22; addresses claim 58). The selection of the polymeric composition to be employed will vary with the site of administration, the desired period of treatment, patient tolerance, the nature of the disease to be treated and the like. Characteristics of the polymers will include biodegradability at the site of implantation, compatibility with the agent of interest, ease of encapsulation and half-life in the physiological environment (see column 5, lines 27-33; addresses claim 58). Biodegradable polymeric compositions may be organic esters, ethers, anhydrides, amides, orthoesters or the like (see column 5, lines 38-53; addresses claim 58). Particles can be prepared where the center may be of one material and the surface have on or more layers of the same or different composition (i.e. jacket surrounding the core comprising a biocompatible membrane; see column 6, lines 15-17; addresses claim 58). Implants may be introduced over or into an avascular region. Surgically-induced avascular regions may be produced in an eye by methods known in the art. Thus, retinal displacement is inherently taught because the implants are surgically induced by sub-retinal implantation known in the art. It may be particularly desirable to produce such an avascular region over or near the desired site of treatment, particularly where the desired site of treatment is distant from the pars plana or placement of the implant at the pars plana is not possible. Introduction of implants over an avascular region will allow for diffusion of the drug from the implant and into the inner eye and avoids diffusion of the

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drug into the bloodstream (i.e. localized retinal detachment; forming a sub-retinal space; see column 6, lines 43-56; addresses claims 11, 20 and 63).

Wong et al. does not specifically teach an injectable solution including the therapeutic medium (claim 1 and 20). Wong et al. also does not specifically teach the polymers polyacrylates, polyvinylidenes, polyvinyl chloride copolymers, polyurethanes, polystyrenes, polyamides, cellulose acetates, cellulose nitrates, polysulfones, polyphosphazenes, polyacrylonitriles, poly(acrylonitrile/covinyl chloride) derivatives, copolymers, and mixtures thereof (claim 58).

Wong'984 teaches intraocular administration of drugs that concentrate the drug at the site of the disease and where biodegradable microcapsules are employed, providing continuous, long-lasting treatment (see abstract and column 3, lines 8-9). Administration may be achieved by injection in a saline solution (see column 7, lines 63-65 and column 9, lines 63-67).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Wong et al. and suspending the microcapsules in a solution because Wong'938 teaches that the biodegradable microcapsules can be injected in a saline solution (see column 7, lines 63-65 and column 9, lines 63-67).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Wong et al. and the specific polymers disclosed in claim 58 because of the following teachings of Wong et al.: 1) the selection of the polymeric composition to be employed will vary with the site of administration, the desired period of treatment, patient tolerance, the nature of the disease to be treated and the like (see column 5, lines 27-33); 2) characteristics of the polymers will include biodegradability at the site of implantation, compatibility with the agent of interest, ease of encapsulation and half-life in the physiological environment (see column 5, lines 27-33); and 3) biodegradable polymeric compositions may be organic esters, ethers, anhydrides, amides, orthoesters or the like (see column 5, lines 38-53). Selection of a known material based on its suitability for its intended use is obvious absent a clear showing of unexpected results attributable to the Applicant's specific selection. See e.g., *In re Leshin*, 227 F.2d 197, 125 USPQ 416 (CCPA 1960).

(2) Claims 5, 19 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. (US 5,869,079) in view of Wong et al. (US 5,632,984; referred to as Wong'984) as applied to claims 1-4, 6, 7, 8, 11, 20, 27, 58-61, 63 and 64 above in view of Hughes et al. (US 5,962,027).

The teachings of Wong et al. and Wong'984 are as applied to claims 1-4, 6, 7, 8, 11, 20, 27, 58-61, 63 and 64 above.

Wong et al. and Wong'984 do not teach a method to specifically treat the ocular diseases ocular neovascularization, ocular inflammation and retinal degeneration.

Hughes teaches surgical techniques, grafts, method for transplanting retinal cells (see abstract in its entirety) for treatment of for use in the reconstruction of a dystrophic retina (see column 2, lines 57-59) such as retinal degeneration (see column 15, example 2, line 37; addresses claims 5 and 19). An instrument is used to detach the retina and then the graft comprising a photoreceptor layer attached to the gelatin substrate is inserted with a tube that comprises a plunger (i.e. injection; see figure 10) into the sub-retinal space to the posterior of the eye (see column 11, lines 62-67 to column 12, lines 1-2). The gelatin serves as a carrier for a number of trophic agents including dexamethasone (see column 7, lines 5-8). Upon dissolution of the substrate, the factor or agent becomes available to impart the desired effect upon the surrounding tissue. The substrate may contain biodegradable polymers to act as slow release agents for pharmacologic substances (see column 7, lines 10-16).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Wong et al. in view of Wong'498 and the specific ocular diseases ocular neovascularization, ocular inflammation and retinal degeneration because of the following teachings: (1) Wong et al. teaches of implants for use in the treatment of ocular conditions, diseases, tumors and disorders (see

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column 6, lines 27-29); (2) ocular neovascularization, ocular inflammation and retinal degeneration are all ocular diseases; (3) Hughes et al. teaches grafts comprising drugs such as dexamethasone for treatment of for use in the reconstruction of a dystrophic retina (see column 2, lines 57-59; column 7, lines 5-8; and see column 11, lines 62-67 to column 12, lines 1-2) such as retinal degeneration (see column 15, example 2, line 37). Thus, implants are known in the art to treat ocular diseases such as ocular neovascularization and retinal degeneration.

(3) Claims 1, 8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Louis (US 5,641,750) in view of Wong et al. (US 5,869,079) in further view of Hughes et al. (US 5,962,027).

Louis teaches a method for treating injury or degeneration of retinal neurons, particularly photoreceptors, by administering glial cell line-derived neurotrophic factor, GDNF (see title and abstract, lines 1-4). The protein product may be administered intraocularly by ocular injection (see column 4, line 66 and column 5, line 15 and claim 18; addresses claim 1). Intraocular systems are those systems which are suitable for use in any tissue compartment within, between or around the tissue layers of the eye itself (i.e. sub-retinally; between the choroid and the retina; see column 18, lines 39-41; addresses claims 1 and 8). A particularly suitable vehicle for intraocular injection is sterile distilled water in which the GDNF protein product is formulated as a sterile, isotonic solution, properly preserved. Yet another ophthalmic preparation may involve

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the formulation of the GDNF protein product with an agent, such as injectable microspheres or liposomes, that provides for the slow or sustained release of the protein which may then be delivered as a depot injection (addresses claim 1). Other suitable means for the intraocular introduction of GDNF protein product includes, implantable drug delivery devices or which contain the GDNF protein product (see column 19, lines 9-19).

Louis does not teach does not teach administration to the posterior segment of the eye by instilling the therapeutic medium sub-retinally between the choroids and the retina. A localized retinal detachment to define the sub-retinal space and disposing the therapeutic medium that space is in taught.

Wong et al. teaches a combinations of hydrophilic and hydrophobic entities in a biodegradable implants that provide controlled, sustained drug release for an extended period of time (see abstract in its entirety; addresses claims 10, 14-16, 27 and 28). Therapeutically active hydrophobic agents, which benefit from release include, non-steroidal anti-inflammatory drugs and steroids of particular interest including cortisone, prednisolone, dexamethasone, fluorometholone (see column 2, lines 63 and 64 to column 3, lines 1-5 and column 8, example 1, lines 23-25; addresses claims 3, 4, 17, 18, 29, and 45). The formulation of implants if for use in the treatment of ocular conditions, diseases, tumors and disorders are of particular interest (see column 6, lines 27-29). Implants are introduced into the suprachoroid may deliver drugs to the choroids

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and the anatomically apposed retina (i.e. localizing the action of the therapeutic medium at the choroids and the retina and minimizing action at other tissues of the eye and forming a depot of a drug between the choroids and the retina; see column 6, lines 38-40; addresses claims 2, 6, 8, 30 and 46). Suitable sites include the posterior chamber with a sub-retinal implantation (see column 6, lines 32, 33 and 61, and 62; addresses claims 1, 7, 10, 11, 12, 14, 16, 20, 25, 26-29, 45 and 46). The implants may be administered by surgical means (i.e. retinal displacement), injection or trocar (see column 7, lines 15 and 16; addresses claims 7 and 12). Implants may be introduced over or into an avascular region. Surgically-induced avascular regions may be produced in an eye by methods known in the art. It may be particularly desirable to produce such an avascular region over or near the desired site of treatment, particularly where the desired site of treatment is distant from the pars plana or placement of the implant at the pars plana is not possible. Introduction of implants over an avascular region will allow for diffusion of the drug from the implant and into the inner eye and avoids diffusion of the drug into the bloodstream (i.e. localized retinal detachment; see column 6, lines 43-56; addresses claims 11, 12, and 14).

Hughes teaches surgical techniques, grafts, method for transplanting retinal cells (see abstract in its entirety) for treatment of for use in the reconstruction of a dystrophic retina (see column 2, lines 57-59) such as retinal degeneration (see column 15, example 2, line 37; addresses claims 5 and 19). An instrument is used to detach the retina and then the graft comprising a photoreceptor layer attached to the gelatin

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substrate is inserted with a tube that comprises a plunger (i.e. injection; see figure 10) into the sub-retinal space to the posterior of the eye (see column 11, lines 62-67 to column 12, lines 1-2; addresses claims 1, 3, 7, 9, 11, 12, 20, 25, 26 and 29).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Louis and administration to the posterior segment of the eye by instilling the therapeutic medium sub-retinally between the choroids and the retina, and further to a localized retinal detachment to define the sub-retinal space because of the following teachings: (1) Louis teaches a method for treating injury or degeneration of retinal neurons, particularly photoreceptors administered via intraocular injection, which is for use in any tissue compartment within, between or around the tissue layers of the eye itself (see column 4, line 66; column 5, line 15; claim 18; and column 18, lines 39-41); (2) Louis also teaches the method can be administered by injectable microspheres or liposomes, that provides for the slow or sustained release of the protein which may then be delivered as a depot injection, or implantable drug delivery devices which contain the GDNF protein product (see column 19, lines 9-19); and (3) Wong et al. teaches formulation of implants for use in the treatment of ocular conditions, diseases, tumors and disorders (see column 6, lines 27-29), wherein the implants are introduced into the suprachoroid to deliver drugs to the choroids and the anatomically apposed retina (i.e. localizing the action of the therapeutic medium at the choroids and the retina and minimizing action at other tissues of the eye and forming a depot of a drug between the choroids and the retina; see

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column 6, lines 38-40); (4) Wong et al. also teaches that suitable sites include the posterior chamber with a sub-retinal implantation (see column 6, lines 32, 33 and 61, and 62), wherein the implants may be administered by surgical means (i.e. localized retinal detachment), injection or trocar (see column 7, lines 15 and 16); and (5) Hughes et al. teaches an instrument that is used to detach the retina and then a graft comprising a photoreceptor layer attached to the gelatin substrate is inserted with a tube that comprises a plunger (i.e. injection; see figure 10) into the sub-retinal space to the posterior of the eye (see column 11, lines 62-67 to column 12, lines 1-2) for the treatment of as retinal degeneration (see column 15, example 2, line 37). Thus, one skilled in the art would be motivated to combine the method of Louis and the administration of the therapy to the particular region of the eye and by a localized retinal detachment because implant injections have been successfully used to treat ocular diseases and disorders in this manner as shown by Wong et al. and Hughes et al.

Response to Arguments

Applicant's arguments filed February 1, 2008 have been fully considered but they are not persuasive, in respect to the 35 USC 103(a) rejection of claims 1, 7, 8 and 11-13 as being unpatentable over Louis in view of Wong et al. in further view of Hughes et al.

Applicant argues that Louis does not teach administration to the posterior segment of the eye by instilling a therapeutic medium sub-retinally, and Wong and/or Hughes does not cure this deficiency. Wong et al. does not teach or suggest injecting a solution and Hughes relates to a method for

the preparation of a graft for transplantation into the subretinal area of a host eye. There is no motivation to combine the teachings of Louis with Wong et al. or Hughes.

The Examiner disagrees because Louis teaches a solution of a therapeutic medium for treating injury or degeneration of retinal neurons applied to the eye via injection or inserts (see column 4, line 66 and column 5, line 15; column 19, lines 9-19 and claim 18). Louis also teaches that the photoreceptors administered via intraocular injection, which is for use in any tissue compartment within, between or around the tissue layers of the eye itself (see column 4, line 66; column 5, line 15; claim 18; and column 18, lines 39-41). The teachings of Wong and Hughes provide teaching of different ways to implant or inject therapeutic mediums as known in the art. Wong et al. also teaches that suitable sites include the posterior chamber with a sub-retinal implantation (see column 6, lines 32, 33 and 61, and 62), wherein the implants may be administered by surgical means (i.e. localized retinal detachment), injection or trocar (see column 7, lines 15 and 16); and (5) Hughes et al. teaches an instrument that is used to detach the retina and then a graft comprising a photoreceptor layer attached to the gelatin substrate is inserted with a tube that comprises a plunger (i.e. injection; see figure 10) into the sub-retinal space to the posterior of the eye (see column 11, lines 62-67 to column 12, lines 1-2) for the treatment of as retinal degeneration (see column 15, example 2, line 37). Thus, one skilled in the art would be motivated to combine the method of Louis and the administration of the therapy to the particular region of the eye and by a localized retinal detachment because implant injections have been

successfully used to treat ocular diseases and disorders in this manner as shown by Wong et al. and Hughes et al.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/K. D. C./
Examiner, Art Unit 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617